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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/482,788	BERKA ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *124-150* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *124-150* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 124-150 are pending.

Applicant's cancellation of claims 98-123 and addition of claims 124-150, in Paper No. 16, filed on 1/28/2003 is acknowledged.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/28/2003 has been entered.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Priority

1. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 09/229862 filed on 1/13/1999.

Claim Objections

2. Claim 124 is objected to because of the following informalities: the term "comprises a modification of a cyclohexadepsipeptide synthetase gene" should be "comprises a modification in a ...gene" or "comprises a modified....gene".

3. Claim 131 is objected to because of the recitation of "parent filamentous fungal cell". While Fusarium venenatum is a filamentous fungal cell, for clarity and consistency, it is suggested that the term be amended to recite "parent Fusarium venenatum cell".

Claim Rejections - 35 USC § 112, Second Paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 124-150 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 124, 137-139, and 150 (claims 125-136, 140-149 dependent thereon) are indefinite in the recitation of "nucleic acid sequence encoding the...polypeptide", "nucleic acid sequence encodes a protease", or "nucleic acid sequence encodes an enzyme selected.." for the following reasons. As known in the art, a sequence is a graphical representation of the order in which amino acid residues or nucleotides are arranged in a nucleic acid or polypeptide molecule. This is analogous to a chemical formula for a chemical compound. Therefore, it is unclear as to how a sequence can encode a molecule. It is suggested that the terms be amended to recite "nucleic acid encoding the...polypeptide", "nucleic acid encodes a protease or "nucleic acid encodes an enzyme selected..". For examination purposes, the proposed language will be used. Correction is required.

6. Claims 124 and 139 (claims 125-138 and 140-150 dependent thereon) are indefinite in the recitation of "(ii) the mutant cell comprises a second nucleic acid sequence which comprises a

modification of a cyclohexadepsipeptide synthetase gene" for the following reasons. First, it is unclear as to how a cell, which is an organism, can comprise a sequence, which as indicated above, is a graphical representation of a molecule. Second, it is unclear as to how a sequence can comprise a modification of a gene. For examination purposes, the term will be interpreted as "(ii) the mutant cell comprises a second nucleic acid wherein said nucleic acid comprises a modified cyclohexadepsipeptide synthetase gene". Correction is required.

7. Claim 131 is indefinite in the recitation of "at least about 25%" since this language is vague and confusing. The use of this language is contradictory because the term "about" can be interpreted as "less than" whereas the term "at least" is synonym of "no less than". For examination purposes, the term will be interpreted as "at least 25%". Appropriate correction is required.

8. Claims 128 and 143 are indefinite in the recitation of "a cyclohexadepsipeptide synthetase which is encoded by a nucleic acid sequence which hybridizes under medium stringency conditions with (i) the nucleic acid sequence of SEQ ID NO: 1, (ii) the cDNA sequence of SEQ ID NO: 1, or (iii) a complementary strand of (i), (ii) or (iii)" for the following reasons. First, for the reasons set forth above, a protein is not encoded by a sequence but rather by a nucleic acid. Furthermore, it is unclear as to how a sequence can hybridize to another sequence since, as known in the art, hybridization takes place between nucleic acid molecules. In addition, "medium stringency conditions" is indefinite absent a statement indicating the hybridization/wash conditions which correspond to "medium stringency". It is noted that the specification discloses at least two different medium stringency conditions (page 22, lines 15-16). Nucleic acids which will hybridize under some hybridization conditions will not necessarily

hybridize under different conditions. Moreover, the term "a complementary strand of (i)...(iii)" is indefinite since it is unclear which complements are encompassed by the claims. Fragments of any size which are complementary to the polynucleotides claimed can be considered as "a complementary strand". Applicants have not define the term "complement", as it relates to size, in the specification either. If the intended complement is the entire complementary strand, the term should be amended to recite "complete complementary strand" or similar. In addition, the term "(iii) complementary strand of (i), (ii) or (iii)" is indefinite since it is unclear as to how (iii) can be a complement of itself. For examination purposes, item (b) of claims 128 and143 will be interpreted as "a cyclohexadepsipeptide synthetase which is encoded by a nucleic acid which hybridizes under any conditions with (i) the nucleic acid of SEQ ID NO: 1, (ii) the cDNA of SEQ ID NO: 1, or (iii) the complete complementary strand of (i) or (ii)". Correction is required.

9. Claims 126, 127, 141, and 142 are indefinite in the recitation of "morphological mutant" as it is unclear what the meaning of the term is within the context of the claims and the specification does not describe the term either. Since the term "morphological" refers to form and structure, it is unclear as to which is the structure in the organism that is mutated. Also, the term "morphological mutant" may refer to the appearance of the cell when grown in culture. For example, certain mammalian cells which are grown in a T flask will attach to the surface and grow as a monolayer whereas others may be grown in suspension. Those grown as a monolayer will have a different shape under the microscope than those grown in suspension. For examination purposes, the term "morphological mutant" will be interpreted as "any mutant". Correction is required.

10. Claim 133 is indefinite in the recitation of "cell comprises at least two copies of the first nucleic acid sequence" since it is unclear as to how a cell can comprise a sequence since a cell is a microorganism and a sequence is a graphical representation of a nucleic acid or a polypeptide, as discussed above. For examination purposes, the term will be interpreted as "cell comprises at least two copies of the first nucleic acid". Correction is required.

11. Claims 136 and 149 (claims 137, 138, 150 dependent thereon) are indefinite in the recitation of "cell further comprises one or more third nucleic acid sequences". Applicants argue that the term "third" is not indefinite because it refers to a third nucleic acid sequence in addition to the first and second sequences already present, and does not refer to a location or position within a structure. These arguments are not found persuasive for the following reasons. The term "third" relates to a specific position or order, therefore it is unclear as to how one can have more than one nucleic acid sequence being "third". If additional nucleic acids are present, these nucleic acids cannot all be "third nucleic acids" but rather, third, fourth, fifth, etc. In addition, as indicated above, it is unclear as to how a cell, which is a microorganism, can have a sequence. If the intended meaning of the term is "cell further comprises one or more nucleic acids in addition to the two nucleic acids already present in the mutant cell of the method of claims 124 or 139", the claim should be amended accordingly. Since it is understood from claims 124 and 139 that the mutant cell already comprises two nucleic acids, claims 136 and 149 may recite "cell further comprises one or more nucleic acids". Dependent claims which further limit the additional nucleic acid may recite "wherein a third nucleic acid...". In the alternative, in addition to amending claims 136 and 149 as suggested, an additional claim may be added further limiting claims which encompass one or more nucleic acids, such that it recites "the ...of

claim.:. wherein a third nucleic acid is present". If the alternative approach is used, dependent claims which further limit the third nucleic acid would have the proper antecedent basis. For examination purposes, the suggested language will be used. Correction is required.

12. Claim 146 is indefinite in the recitation of "the mutant cell of claim 139 wherein the Fusarium venenatum cell comprises.." as it is unclear if the limitation refers to the mutant Fusarium venenatum cell or the parent Fusarium venenatum cell. For examination purposes, it will be assumed that the limitation refers to the mutant Fusarium venenatum cell. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 124-128, 131-143, 146-150 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 124-127, 131-138 are directed to a method of producing a secreted polypeptide using a genus of mutant F. venenatum cells wherein said cells comprise a genus of modified cyclohexadepsipeptide synthetase genes, wherein said genes have been modified in any way and wherein said genus of mutant cells produce less cyclohexadepsipeptides than the parent F.

venenatum cells from which they derive due to any modification in said cells. It is noted that claims 124 and 139 do not indicate that the reduction in cyclohexadepsipeptide production is due to the presence of a modified cyclohexadepsipeptide synthetase gene. Claim 128 is directed to the method of claim 124 with the added limitation that the gene encoding the cyclohexadepsipeptide synthetase should hybridize to the polynucleotide of SEQ ID NO: 1 under any conditions. Claim 131 adds the limitation that the mutant cell produces at least 25% less cyclohexadepsipeptide than the parent fungal cell. Claims 139-142, 146-150 are directed a genus of mutant F. venenatum cells which comprises a genus of modified cyclohexadepsipeptide synthetase genes, wherein said genes have been modified in any way and wherein said mutants produce less cyclohexadepsipeptides than the parent F. venenatum cell from which they derive due to any modification in said cells. Claim 143 is directed to the mutant cell of claim 139 with the added limitation that the gene encoding the cyclohexadepsipeptide synthetase should hybridize to the polynucleotide of SEQ ID NO: 1 under any conditions.

While the specification discloses the F. venenatum cyclohexadepsipeptide synthetase of SEQ ID NO: 2 and its corresponding nucleic acid (SEQ ID NO: 1), there is no disclosure of other cyclohexadepsipeptide synthetase genes from other organisms as encompassed by the claims. Also, there is no disclosure of the critical structural elements required in a polynucleotide to encode a cyclohexadepsipeptide synthetase nor there is disclosure of the structural elements related to cyclohexadepsipeptide synthetase function required in a polynucleotide which hybridizes under any conditions to a polynucleotide which encodes a 70% sequence homolog of the polypeptide of SEQ ID NO: 2. Furthermore, with the exception of a deletion in the polynucleotide of SEQ ID NO: 1, there is no disclosure of additional mutations

in a Fusarium venenatum cell which would result in any reduction in the production of cyclohexadepsipeptides, including a 25% reduction, as recited. Similarly, with the exception of a deletion in the polynucleotide of SEQ ID NO: 1, there is no disclosure of other modifications in a cyclohexadepsipeptide synthetase gene.

The argument can be made that the genes of the instant claims are adequately described since one can isolate these genes by sequence comparison using the polynucleotide/polypeptide structures disclosed in the instant application or the prior art, the state of the art teaches that sequence comparison alone should not be used to determine function and that small structural changes can drastically change function. Bork (Genome Research, 10:398-400, 2000) teaches protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* where found to be hydroxylases once tested for activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. The specification only discloses a single species of the genera of genes and modifications which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of

all species within the genus claimed. Thus, one skilled in the art cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

15. Claims 124-128, 131-143, 146-150 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a method for producing a secreted heterologous polypeptide using a Fusarium venenatum cell, wherein the cell has been transformed such that said cell comprises a polynucleotide encoding the cyclohexadepsipeptide synthetase of SEQ ID NO: 2, wherein said polynucleotide has been modified by a deletion such that an inactive cyclohexadepsipeptide synthetase is produced, and wherein said modification results in the production of less cyclohexadepsipeptides when compared with the untransformed parent (i.e. wild-type) Fusarium cell, and (2) a Fusarium venenatum cell, wherein the cell has been transformed such that said cell comprises a polynucleotide encoding the cyclohexadepsipeptide synthetase of SEQ ID NO: 2, wherein said polynucleotide has been modified by a deletion such that an inactive cyclohexadepsipeptide synthetase is produced, and wherein said modification results in the production of less cyclohexadepsipeptides when compared with the untransformed parent (i.e. wild-type) Fusarium cell, does not reasonably provide enablement for (1) a method for producing a secreted heterologous protein using any mutant Fusarium venenatum cell which has been modified in any way to produce less cyclohexadepsipeptide synthetase and further comprises any cyclohexadepsipeptide synthetase gene, any cyclohexadepsipeptide synthetase polynucleotide encoding a 70% sequence homolog of the polypeptide of SEQ ID NO: 2, or any cyclohexadepsipeptide synthetase polynucleotide which hybridizes under any conditions to a polynucleotide encoding a 70% sequence homolog of

the polypeptide of SEQ ID NO: 2, wherein said gene or polynucleotide has been modified in any way, or (2) any mutant Fusarium venenatum cell which has been modified in any way to produce less cyclohexadepsipeptide synthetase and further comprises any cyclohexadepsipeptide synthetase gene, any cyclohexadepsipeptide synthetase polynucleotide encoding a 70% sequence homolog of the polypeptide of SEQ ID NO: 2, or any cyclohexadepsipeptide synthetase polynucleotide which hybridizes under any conditions to a polynucleotide encoding a 70% sequence homolog of the polypeptide of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims, as described above, is not commensurate with the enablement provided due to the large number of unknown cyclohexadepsipeptide synthetase genes/polynucleotides and modifications encompassed by the claims. While the polypeptide of SEQ ID NO: 2 and its corresponding polynucleotide have been disclosed, there is no disclosure of (1) other cyclohexadepsipeptide synthetase genes, (2) structural elements which are required in any polynucleotide to encode a cyclohexadepsipeptide synthetase, (3) amino acids in the polypeptide of SEQ ID NO: 2 which can be deleted, substituted or inserted to create a 70% structural homolog with cyclohexadepsipeptide synthetase activity, or (4) structural elements

related to cyclohexadepsipeptide synthetase function required in a polynucleotide which hybridizes under any conditions to a polynucleotide which encodes a 70% structural homolog of the polypeptide of SEQ ID NO: 2. Furthermore, the specification is silent in regard to other modifications in a mutant Fusarium venenatum cell which can lead to less production of cyclohexadepsipeptides, such as inactivation of other genes involved in the biosynthesis of cyclohexadepsipeptides, or other modifications in a cyclohexadepsipeptide synthetase gene, such as mutations in the regulatory elements of the gene which would result in reduced expression of said gene. In addition, as indicated above, while one could argue that the genes required in the claimed invention can be isolated by structural homology, the state of the art teaches the unpredictability of such approach, as evidenced by Bork, Broun et al., Witkowski et al., Van de Loo et al. and Seffernick et al. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to display the desired function, and the unpredictability of the prior art in regard to annotation of function based on structural homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to (1) isolate other cyclohexadepsipeptide synthetase genes, (2) isolate and test polynucleotides encoding polypeptides having at least 70% sequence identity to the polypeptide of SEQ ID NO: 2, (3) isolate and test polynucleotides which hybridize under any conditions to polynucleotides encoding polypeptides having at least 70% sequence identity to the polypeptide of SEQ ID NO: 2, and (4) find other modifications in a Fusarium cell or in a cyclohexadepsipeptide synthetase gene which would result in less production of cyclohexadepsipeptides. Thus, Applicant has not provided sufficient guidance to

enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

16. In Paper No. 13, filed on 10/29/2002, Applicants submitted an amendment which added claims 98-123. In the Advisory Action (Paper No. 14), mailed on 11/27/2002, Applicants were advised that claims 98-123 would be rejected under 35 USC 112, first paragraph for the reasons of record.

17. Applicants argue that the specification provides a written and enabling description as to how to produce mutant cells from a parent Fusarium venenatum cell by deleting or disrupting a nucleic acid encoding a cyclohexadepsipeptide synthetase in the parent cell and how to express a secreted heterologous protein in such cell. With this information and the knowledge available to one of skill in the art, one can construct deletion or disruption vectors to disrupt or delete a cyclohexadepsipeptide synthetase gene without knowledge of the gene's sequence. Furthermore, Applicants assert that it is well known in the art that by selecting a conserved or homologous region of a known gene based on sequence comparisons to other similar genes, one can disrupt the corresponding gene, using for example, homologous recombination. Applicants argue that the specification provides a cyclohexadepsipeptide synthetase gene of SEQ ID NO: 1, which shares approximately 59% identity to the esyn1 gene of Fusarium scirpi, and that a sequence comparison of both sequences indicates regions of conserved homology between the sequences at the DNA level which can be used to construct disruption/deletion vectors for another Fusarium venenatum cell without any knowledge of the DNA sequence in that cell. Applicants submit the teachings of Herrmann et al., as evidence to support their argument.

18. While Applicant's arguments relate to rejections of claims which are now cancelled, they have been considered since they are still applicable to some of the new claims as set forth in the rejections applied above. While the Examiner acknowledges the teachings of Herrmann et al. and agrees that one can use homologous recombination, deletion or disruption vectors to inactivate a gene, it is noted that the claims as written are not limited in regard to the method used for reducing the expression of a cyclohexadepsipeptide synthetase gene. See rejections above for claim interpretation and discussion. As indicated above, the claims are drawn to a method wherein the cyclohexadepsipeptide synthetase gene is modified in any way and wherein the Fusarium venenatum cells is modified in any way to produce less cyclohexadepsipeptides than the unmodified parent Fusarium venenatum cell. There is no recitation in the claims which indicates that the reduction in cyclohexadepsipeptides is due to the deletion or disruption of the cyclohexadepsipeptide synthetase gene. Therefore, as indicated above, other modifications such as disruption of other genes involved in cyclohexadepsipeptide synthesis or mutations in the regulatory elements of the gene which would reduce expression have not been disclosed. In regard to the teachings of Herrmann et al., it is noted that in view of the unpredictability of the art already discussed and the teachings of the specification, there is no evidence which indicates that conserved regions between the cyclohexadepsipeptide synthetase genes of Fusarium avenaceum and Fusarium scirpi are also conserved regions among all Fusarium cyclohexadepsipeptide synthetase genes, nor there is any teaching or suggestion as to which of these conserved regions correlate with function. See claim interpretation and discussion above. Therefore, for the reasons set forth above, Applicant's arguments are not deemed persuasive to

avoid the 35 USC 112, first paragraph rejections applied to the newly added claims as already discussed.

Claim Rejections - 35 USC § 103

19. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

20. Claims 70-72, 77-78, 80, 86-87, 91-93, and 95 were rejected under 35 U.S.C. 103(a) as being unpatentable over Herrmann et al. (Molecular Plant-Microbe Interactions 9:226-232, 1996; cited in the IDS) in view of Tsuchiya et al. (Appl. Microbiol. Biotechnol. 40:327-332, 1993).

21. This rejection has been discussed at length in Paper No. 10 mailed on 4/23/2002.

22. Applicants argue that none of the references cited teach either alone or in combination, a method for the production of secreted polypeptides in a cyclohexadepsipeptide synthetase-deficient Fusarium venenatum cell or a cyclohexadepsipeptide synthetase-deficient Fusarium venenatum cell. As such, Applicants request the withdrawal of the rejection.

23. While claims 70-72, 77-78, 80, 86-87, 91-93, and 95 have been canceled, Applicant's arguments have been fully considered in regard to newly added claims 124-150. In view of the fact that the claims are now drawn to (1) a method for the production of secreted proteins using a mutant Fusarium venenatum cell which is capable of producing less cyclohexadepsipeptides or to (2) a mutant Fusarium venenatum cell which is capable of producing less cyclohexadepsipeptides, and since the cited references do not teach, either alone or in combination, the invention of newly added claims 124-150, this rejection is hereby withdrawn.

Conclusion

24. No claim is in condition for allowance.

25. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

26. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
June 19, 2003

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600